

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US03/36292

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : C07K 14/00

US CL : 435/69.7

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/69.7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Continuation Sheet

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,843,724 A (KRUG et al.) 01 December 1998 (01.12.1998), see the claims.	1-4, 8, 9, 11, 12
Y	WANG et al. The RNA-Binding and Effector Domains of the Viral NS1 Protein Are Conserved to Different Extents among Influenza A and B Viruses. <i>Virology</i> . 1996, Vol. 223, pages 41-50, see the abstract.	1-4, 8, 9, 11, 12
Y	RYTER et al. Molecular basis of double-stranded RNA-protein interactions: structure of a dsRNA-binding domain complexed with dsRNA. <i>The EMBO Journal</i> . 1998, Vol. 17, No. 24, pages 7505-7513, see the entire document.	1-4, 8, 9, 11, 12
Y	LU et al. Binding of the Influenza Virus NS1 Protein to Double-Stranded RNA Inhibits the Activation of the Protein Kinase That Phosphorylates the eIF-2 Translation Inhibition Factor. <i>Virology</i> . 1995, Vol. 214, pages 222-228, see the abstract.	1-4, 8, 9, 11, 12

Further documents are listed in the continuation of Box C.

See patent family annex.

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*B\* earlier application or patent published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

16 July 2004 (16.07.2004)

Date of mailing of the international search report

06 AUG 2004

Name and mailing address of the ISA/US

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**Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-4, 8, 9, 11, 12

Remark on Protest

  

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/36292

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-4, 8, 9, 11, 12, drawn to a composition comprising a reaction mixture wherein the NS1 is protein of Influenza A.

Group II, claim(s) 1, 5-8, 10-12, drawn to a composition comprising a reaction mixture wherein the NS1 is protein of Influenza B.

Group III, claim(s) 13-31, drawn to method of identifying compounds having inhibitory activity against influenza virus.

Group IV, claim(s) 32-34, drawn to method of identifying compounds having inhibitory activity against influenza virus via NMR.

Group V, claim(s) 35-37, drawn to method of preparing a composition for inhibiting replication of influenza virus.

Group VI, claim(s) 38-42, drawn to method of identifying compounds having inhibitory activity against influenza virus via crystallography.

The inventions listed as Groups I-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The invention of Group I is known in the prior art as evidence by Wang et al (Virology, 1992, Vol. 223, pp. 41-50) wherein the reference teaches NS1 domain of influenza A and its binding to dsRNA (see the abstract); or see Lu et al (Virology, 1995, Vol. 214, pp. 222-228) wherein the NS1 protein binding to dsRNA is taught (see the abstract). The cited evidence proves that the technical feature of Group I does not make a contribution over the prior art. Thus, the claims are not so linked by a special technical feature within the meaning of PCT Rule 13.2.

**Continuation of B. FIELDS SEARCHED Item 3:**  
WEST, NPL, EPA, JPA, BIOSIS, CAPLUS, MEDLINE  
search terms: influenza virus, NS1, dsRNA, NS1B